Development of a Smart Holmium:YAG Laser Lithotriptor

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Background and Objective: **The purpose of this study was to develop a feedback control system for the pulsed holmium: YAG medical laser that enhances tissue selectivity and safety by discriminating between soft and hard biological tissue such as urinary and biliary calculi and bone.**
Study Design/Materials and Methods: **The ability to discriminate is achieved by monitoring prompt laser-induced visible/NIR photoemissions via retrograde transmission over the laser delivery fiber in conjunction with a developed detection algorithm.**
Results: **Experimental data are presented for a system that employs this discrimination scheme with an electro-optic shutter for rapid intrapulse feedback control of holmium laser-based lithotripsy procedures. The results demonstrate the feasibility of a lithotriptor that can deliver 1 J per pulse to calculi yet limit errant discharges to surrounding urinary tract tissue to $\leq$ 0.1 J.**
Conclusion: **Based on animal tissue safety data, the laser margin of safety is improved by an order of magnitude. Lasers Surg. Med. 21:20–28, 1997**

Key words: feedback control; optical emission; electro-optic shutter

INTRODUCTION

The use of the laser as a minimally invasive technique for laser lithotripsy is now a clinically accepted procedure. Recently, the pulsed Ho:YAG laser was approved by the FDA for use as an endoscopic lithotripsy device. Laser lithotripsy's principal advantage over other endoscopic techniques such as ultrasonic and electrohydraulic probes is its ability to deliver and pinpoint energy on the calculus using very small diameter and flexible optical fibers, thus minimizing errant energy deposition onto the ureter.

Over the past few years there has been a growing appreciation within the laser surgery community of the benefits of pulsed versus continuous wave (cw) lasers for more controlled and precise tissue removal. Ablation procedures that may have been performed in the past with CO_2, argon, or cw Nd:YAG lasers are now increasingly being performed with new pulsed lasers. A notable example of such a laser is the pulsed holmium solid state laser operating at 2.1 μm. This laser has recently become of great interest for applications in orthopedic [1], vascular [2], urologic [3,4], and otolaryngolic [5,6] surgery. Manufacturers' estimates [7] indicated that by the end of 1993, there was a total of some 400 holmium lasers placed at U.S. hospitals and outpatient surgery centers.

The holmium laser offers numerous advantages, which include: (1) high energy, high peak power (several kW) pulses, (2) a wavelength (and pulse duration) that is readily transmitted down

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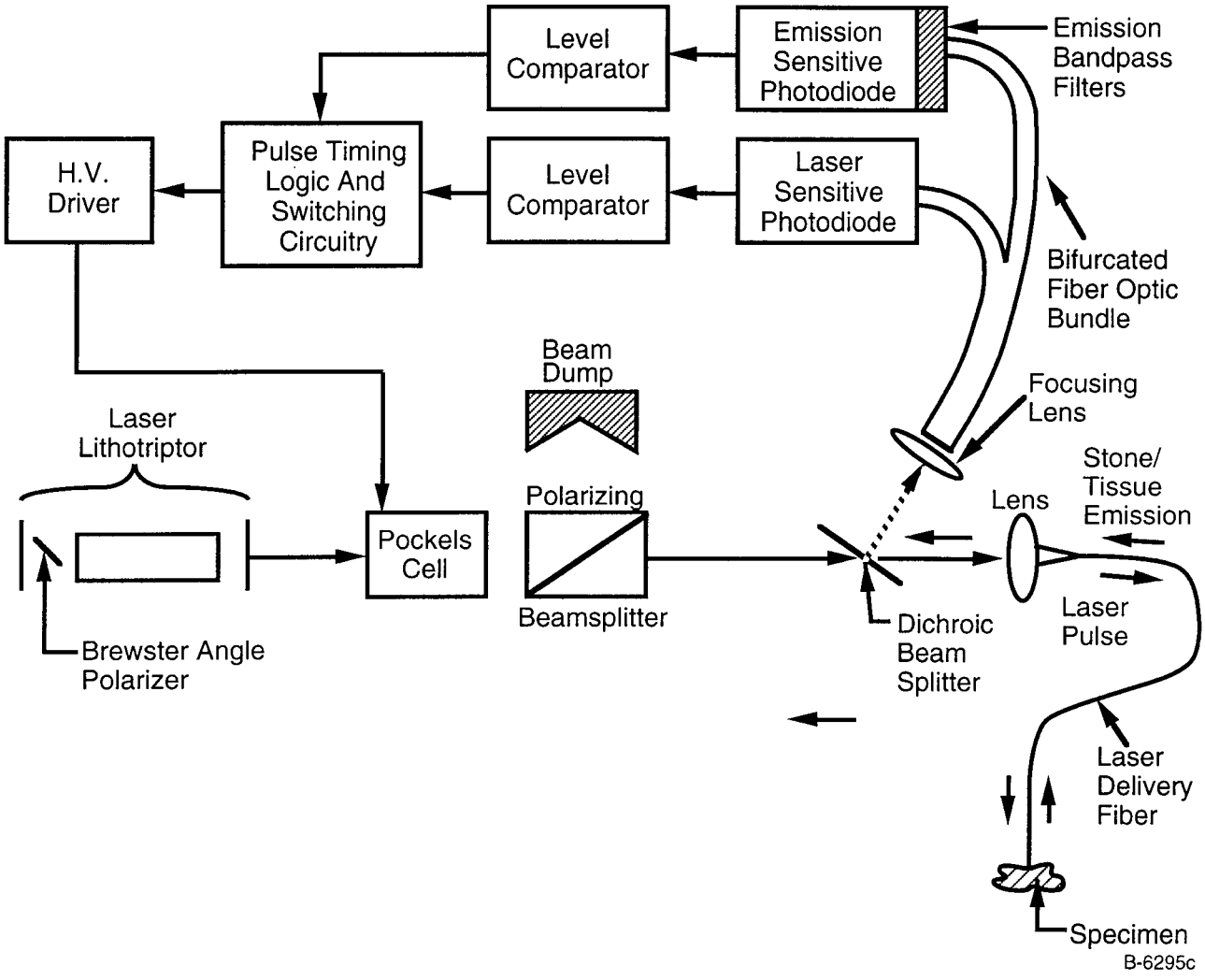

Fig. 1. Schematic diagram of intrapulse feedback control system for laser lithotriptor.

flexible quartz fibers, (3) an absorption depth (≈300 μm) that allows it to be efficiently absorbed by most biological tissues, yet penetrate deep enough to be hemostatic, and (4) it is a solid-state laser that is relatively inexpensive and easy to maintain. In addition to ablating soft tissue effectively, the holmium laser can also efficiently and cleanly ablate bone [5], calculi [3,4], and other hard tissues. This potential for multiple applications in the surgical suite is another feature that makes the holmium laser so attractive, particularly in light of the demand for more cost-effective health care delivery.

This characteristic of the holmium laser being a "nondiscriminating" tissue ablator can also be a disadvantage. This is illustrated by two recently reported investigations of the holmium laser for endoscopic lithotripsy [3,4]. Whereas both of these studies concluded that, when delivered via a 400 μm fiber, the holmium laser can effectively be used to break up urinary calculi, they also cautioned that extreme care must be exercised to avoid laser damage to surrounding urinary tract tissue. This was shown to be particularly true when operating the holmium laser at energies above 0.5 J per pulse. Such energies are required to achieve desirable stone fragmentation rates, particularly for harder stones such as calcium oxalate monohydrate (COM) and dense cystine stones. In fact, to achieve stone fragmentation efficacies approximating that of the pulsed-dye laser, Watson [4] has found that an energy of 1 J per pulse is needed. We believe the solution to the safety problem is efficient feedback control.

Figure 1 presents a schematic diagram of the "smart" laser system under development. Figure

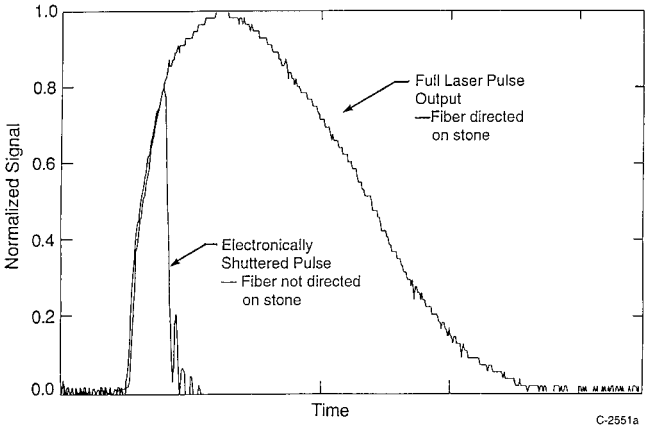

Fig. 2. Bimodal pulse output of "smart" pulsed laser lithotriptor.

2 shows the two modes of pulse output that it would deliver as a lithotriptor where the transmitted energy, when the laser is not on a stone, will be automatically reduced. To support this, we present data that strongly indicate that the system under development will deliver > 1 J per pulse to calculi yet limit errant laser discharges to surrounding soft tissue to $\lesssim$ 0.12 J. This will improve (by more than a factor of 10) the margin of safety associated with performing holmium laser lithotripsy.

Preliminary data are already available that can be used to estimate the improvement in tissue safety that can be achieved. Such data are found in the published work of Sayer et al. [3] in which the number of holmium pulses required to achieve intentional ureteral wall perforation were measured as a function of pulse energy. These data are plotted in Figure 3, along with data from Ref. [8], and clearly illustrate the substantial improvement in tissue safety that results as the pulse energy the tissue is exposed to is decreased, e.g., from under 10 pulses required for a wall perforation at 1 J per pulse to ~ 50 pulses required to perforate at 0.5 J per pulse. A conservative extrapolation of these results indicates that if, under similar conditions, the pulse energy exposure can be reduced to only 0.1 J, > 250 pulses at the same site would be required to cause a wall perforation. At a pulse repetition frequency of 5 Hz, this corresponds to a required exposure time of > 50 seconds. As part of our studies, we performed independent experiments to confirm the relative enhancement in tissue safety that results as the pulse energy exposure is decreased.

Over the past few years, several groups [9–12] have developed approaches for "smart" laser lithotriptors based on various stone/soft tissue detection algorithms. Most of these efforts to date have focussed on approaches that work with the pulsed dye laser lithotriptor (λ = 504 or 590 nm), although researchers in Germany also have recently applied their "stone/tissue detection system" to a microsecond pulse duration alexandrite laser lithotriptor (λ = 780 nm) [12]. We are aware of no published work involving similar efforts to develop a "smart" holmium laser lithotriptor that emits at a considerably longer wavelength and pulse duration than these other lithotriptors.

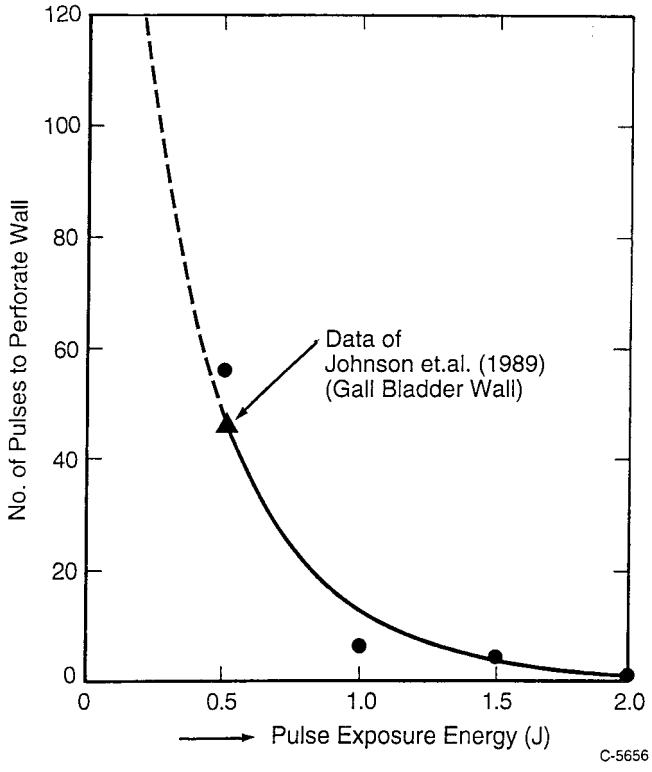

Fig. 3. Number of holmium laser pulses required to perforate fresh, ex vivo human ureter (tangential contact, 400-μ fiber, 5-Hz PRF) (from Sayer et al., 1993).

MATERIALS AND METHODS

To demonstrate the feasibility of a "smart" Ho:YAG laser lithotriptor, several tasks were conducted. A discussion follows on these tasks and the research methods employed for their accomplishment.

Tissue Photoemission Experiments (In Vitro Studies)

The specific visible and near infrared (NIR) photoemissions generated from in vitro pulsed Ho:YAG laser irradiation of urinary and biliary

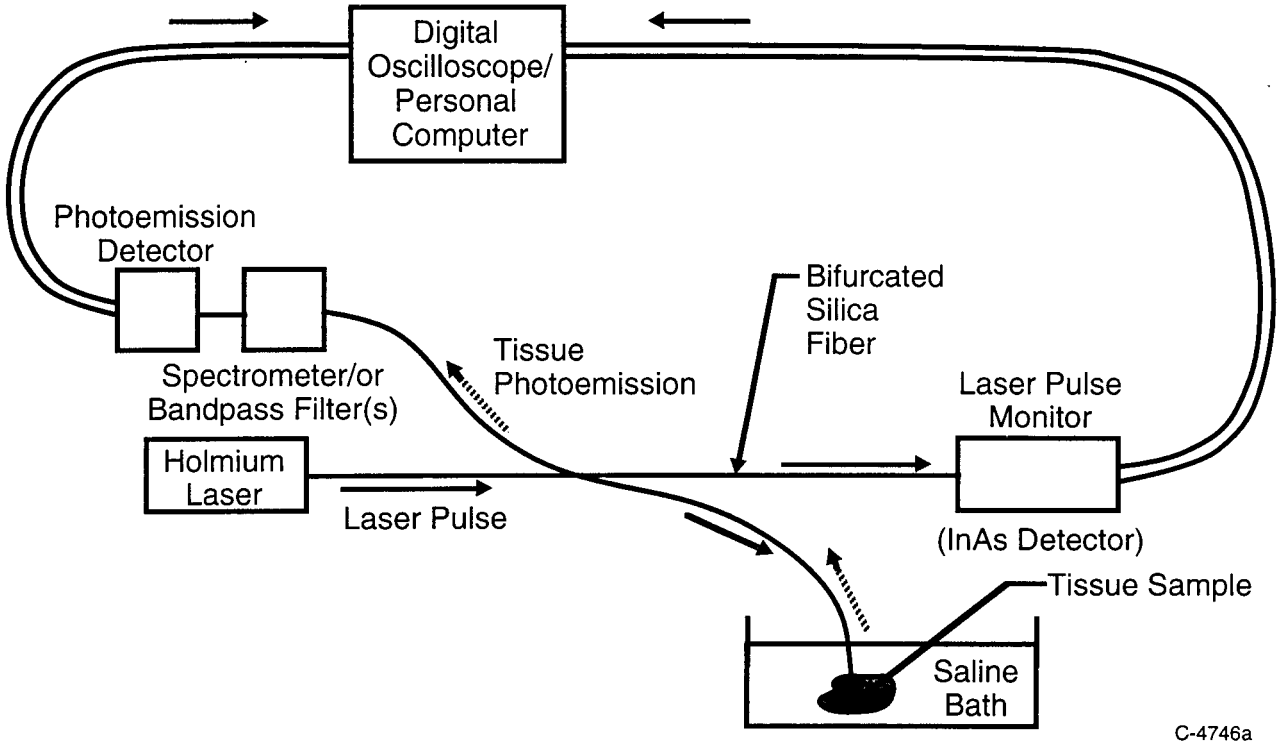

Fig. 4. Schematic diagram of experimental setup for tissue photoemission studies.

stones, excised soft tissue, bone and cartilage specimens, and blood were measured. Multiple stone samples of various types were obtained from a supply salvaged from past surgical procedures and characterized by the Stone Analysis Laboratory (Newton, MA). For this testing a stone sample of each type was chosen at random from this supply. In vitro tissue samples consisted of freshly excised sections of porcine or bovine anatomical parts obtained from a licensed slaughterhouse. Blood samples were obtained from a human volunteer. All in vitro stone and tissue specimens were irradiated under normal saline.

The laser and optical detection apparatus used to acquire the laser-induced photoemission data is illustrated in Figure 4. The laser was a VersaPulse Model 2.1 pulsed Ho:YAG laser by Coherent. The laser energy was delivered to the test samples via a custommade, bifurcated fiber assembly fabricated from 400 μm core, low OH fused silica fiber. Specimen optical emissions were transmitted retrograde over the fiber assembly and then split off to an optical detection system for spectral and/or temporal analysis. All samples were irradiated under saline with direct fiber contact. Spectral data were obtained using a gated diode array spectrograph with a spectral resolution of ~ 0.5 nm per pixel. A total of 77 tests were conducted using 14 different materials to obtain the spectral data. Emission and onset times were obtained using a single silicon photodiode equipped with a bandpass filter with a cut-on wavelength of 585 nm, thus integrating all emitted light from 585 nm to ~ 1,100 nm. A total of 36 tests were conducted to determine the emission and onset times for 11 different material types. Each sample was irradiated with a sequence of between 8 and 15 laser pulses. Reference laser pulse temporal waveforms were also recorded for each emission trace using a high speed room temperature InAs detector. All emission data were digitized and stored on a computer for subsequent analysis.

In Vivo Animal Studies (Tissue Safety and Photoemission Experiments)

A series of in vivo animal studies were performed in the urinary tract of a laboratory rabbit. The objective was to obtain an assessment of improved tissue safety that results as the energy per pulse discharged on the tissue is decreased. The other purpose of the in vivo studies was to acquire photoemission data from live urinary tract tissue to test the validity of earlier in vitro results [3,4].

The in vivo tests were carried out at the Lahey Clinic Laser Research Laboratory.

Animal protocol. An adult, 4 kg, female laboratory rabbit was anesthetized by intramuscular injection of a "cocktail" consisting of a Ketamine HCl (100 mg/ml) and Xylazine (20 mg/ml) drawn up and mixed together at 35 mg Ketamine/kg body weight, 5 mg Xylazine/kg body weight. Anesthesia was maintained with halothane and a mechanical respirator.

A midline incision was made to deliver the bladder on to the abdominal surface. A 1 cm cystotomy was made to insert a continuous flow resectoscope sheath. A specially designed flat ended urethrotome sheath was used in conjunction with a specially designed introducer element that guided the holmium laser fiber to the bladder wall at the desired position. Purse string sutures were used to secure the bladder around the scope sheath. A video camera was then attached to the telescope. Under direct vision with the bladder distended to 75 cc, continuous flow with saline was used to give good visualization and to mimic bladder distention as occurs in a standard cystoscopic evaluation. The laser fiber was then positioned perpendicular in such a way that the tip touched the wall of the bladder with minimal applied pressure. The laser was then fired at a fixed pulse energy setting and pulse repetition frequency of 5 Hz until perforation of the bladder wall was visually observed. With the assistance of slow motion video replay, the number of pulses needed to cause a perforation was then determined and tabulated as a function of the pulse energy setting. To obtain pulse energies < 500 mJ, calibrated beam splitting attenuators were placed in the beam path. The output pulse energy was measured using a commercial laser power meter.

Following completion of the closed bladder experiment, the bladder was then opened and sutured to the anterior abdominal wall and irrigated with a constant drip of saline. The laser delivery fiber was then replaced with the bifurcated fiber used in the tissue photoemission studies and the filtered photodiode detection system coupled to the free proximal end. Under direct vision the distal fiber tip was then placed directly on the bladder wall and the laser fired to record the photoemissions induced. The resulting emission signals were recorded using a digital storage oscilloscope.

Immediately following these procedures, the rabbit was sacrificed by intracardiac injection of 1 ml of sodium pentobarbital (390 mg/ml).

Electro-optic Shuttering of Holmium Laser Pulse

An experiment was carried out to demonstrate the feasibility of rapidly terminating the holmium laser beam intrapulse. To accomplish this, the laser beam was first linearly polarized by passing it through a polarizing cube made of Calcite. This cube reflects out of the beam propagation path all of the rejected polarization states except the selected one that is transmitted. This linearly polarized beam was then passed through an electro-optical modulation device called a Pockels cell.

The operation of a Pockels cell is based on an electrically-induced (voltage potential) change in the birefringence of a crystal. This results in the change, commonly referred to as the rotation, of the polarization of the propagating light. For the Ho:YAG wavelength of 2.1 μm, a Pockels cell made of lithium niobate was used. The Pockels cell was then followed in the optical train by a second Calcite polarizer cube. This Pockels cell used in combination with this second cube comprises the fast shutter for the linear polarized beam.

Under normal operating conditions, the voltage setting and resulting polarization phase of the Pockels cell and orientation of the second calcite polarizer were set to allow maximum transmission of the linearly polarized beam. Thus at the start of each pulse, the beam shutter was enabled for maximum transmission. To close the shutter during the pulse, a trigger pulse was sent, at a selected delay time, to the Pockels cell voltage driver, which switched the applied voltage to zero. This resulted in the Pockels cell rotating the beam polarization vector by 90°, thereby closing the shutter.

RESULTS

Calculus and Tissue Photoemission Measurements

The first measurements were to record, using the gated diode array spectrograph, the visible and NIR spectral emissions induced by holmium laser irradiation of various calculi and soft tissue samples. In Figure 5 we compare the results obtained from a calcium oxalate stone to that from a bovine bladder wall in vitro. The gated spectra shown were obtained 90 μs after the start of the laser pulse. Note the strong emission from the calculus and the virtually absent emission from the bladder wall. Similar experiments

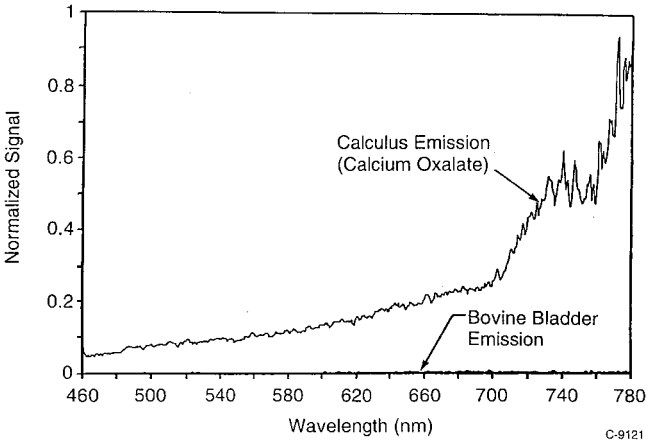

Fig. 5. Spectrally resolved laser-induced photoemission from urinary calculus and soft tissue (t(delay) = 90 μs, Ep = 0.8 J).

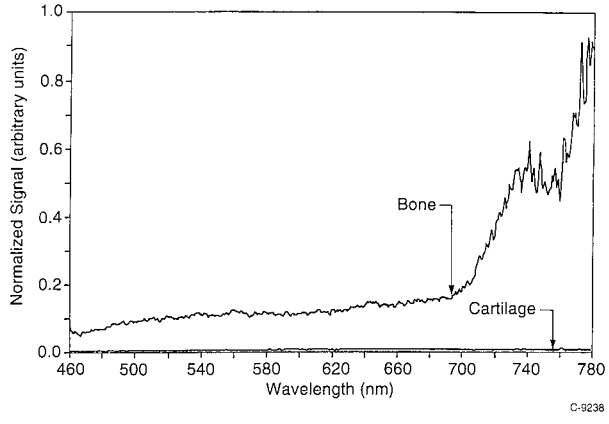

Fig. 6. Spectrally resolved, laser-induced photoemission from bovine ankle bone and ankle cartilage (t(delay) = 90 μs, Ep = 0.8 J).

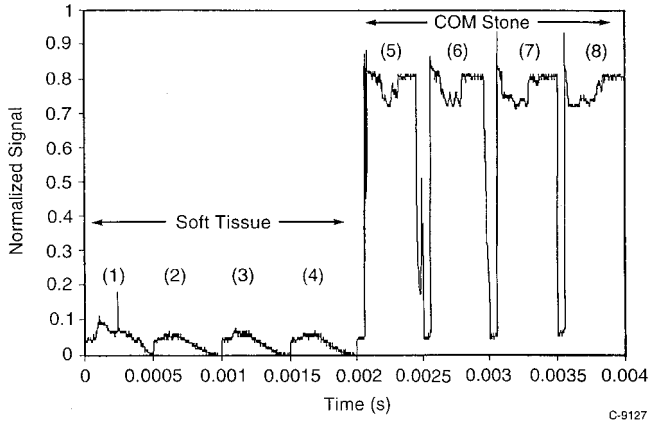

Fig. 7. Sequence of holmium laser-induced emission pulses; pulses from 1–4 from soft tissue sample; pulses 5–8 from calcium oxalate stone; laser energy ≈ 0.8 J/pulse.

were performed for a variety of calculi, soft tissue specimens, and blood and saline. The consistent result found was that the soft tissues, blood and saline produced negligible visible/NIR emission, whereas calculi produced very strong emissions consisting primarily of continuum emission peaking in the near infrared. We believe the origin of this emission is incandescence.

In Figure 6, we present the results of similar measurements obtained for bovine ankle bone and ankle cartilage. Note the very strong emission from the bone, very similar to that found for the calculi, and the much weaker emission from the cartilage. It also should be noted that whereas weak compared to the emission from bone, the cartilage emission was measurable above the background and clearly greater than that observed from the softer tissues (bladder and bovine ankle flesh), blood, or saline.

Measurements were also performed in which the spectrograph was replaced by a single silicon photodiode with a long wavepass filter to conveniently monitor the emission amplitude time histories. Figure 7 displays the emission signals seen for a sequence of laser discharges. The first four are from discharging the laser on a rabbit bladder in vivo; the last four are from discharges on a urinary stone. Note again the very strong emissions from the calculus—strong enough to easily saturate the photodetector—and the essentially negligible emission from the soft tissue.

In Figure 8, individual photoemission signals from the calculus and the rabbit bladder are plotted on an expanded time scale and displayed in relation to the laser pulse time history. Here, we see that there is a clearly definable delay or induction time of ~ 25 μs until the onset of strong stone emission. This delay time determines how quickly stone detection can be confirmed. Similar measurements were repeated for a variety of stone types (as well as bone) and the results are summarized in the bar charts of Figures 9 and 10.

Figure 9 summarizes the induction times to strong emission onset measured for various calculi. Note that with the exception of the pure uric acid calculi (6–8% of the urinary stone population), induction times are all under 80 μs. In Figure 10, we convert these measured induction times to equivalent induction energies. These are essentially the energies that were deposited before strong calculus emission was observed. Note again that with the exception of uric acid stones, the induction energies are all less or equal to 120 mJ. This means that for the great majority of stones, determining whether the laser is being

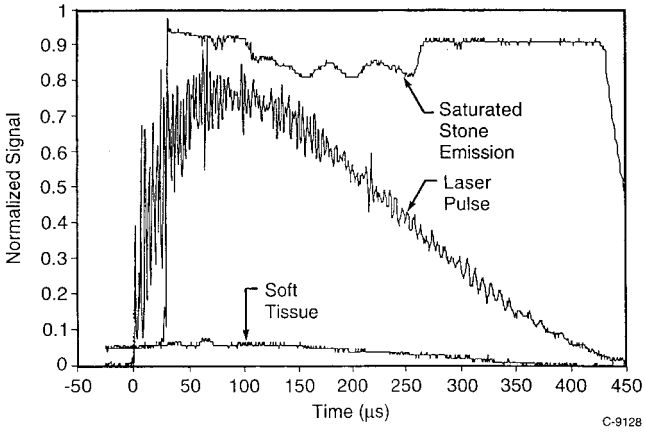

Fig. 8. Comparison of tissue photoemission and holmium laser pulse history; laser energy ≈ 0.8 J/pulse.

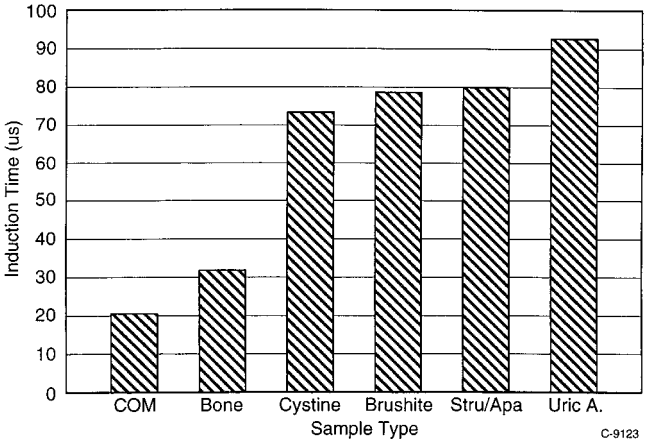

Fig. 9. Pulse mean induction time to "strong" emission onset.

discharged on the calculus (and then closing a fast beam shutter if it is not), should be possible within the first 120 mJ or less of energy discharge. This provides a significant safety margin as demonstrated next.

Tissue Safety Results

To quantify how reducing the pulse energy exposure risk to urinary tract tissue can increase the margin of tissue safety, we performed in vivo tissue safety studies in the rabbit bladder. The results obtained are summarized in Figure 11. The number of pulses required to cause a wall perforation are plotted as a function of the energy per pulse discharged. The laser was operated at a pulse repetition frequency of 5 Hz. When decreasing the energy per pulse discharged on the tissue, the number of pulses required to cause a perforation increases from only 3 or 4 pulses, or $\leqslant$ 0.8 seconds exposure time, at 800 mJ per pulse, to > 40 pulses, or $\geqslant$ 8 seconds exposure time, at 120 mJ per pulse. Thus the margin of safety against laser tissue injury can be improved by more than a factor of 10!

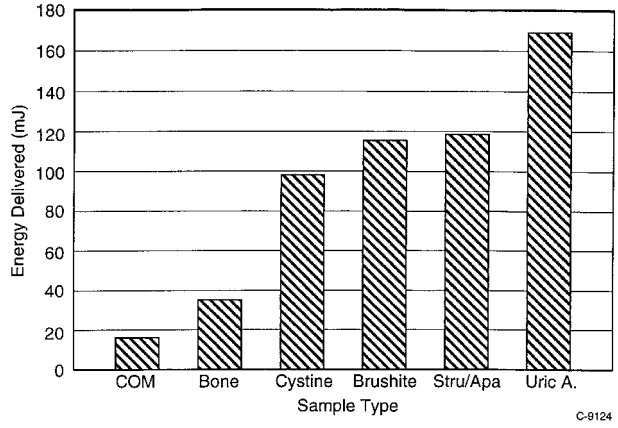

Fig. 10. Mean pulse energy delivered up to "strong" emission onset.

Intrapulse Shuttering Results

The last set of experiments performed were to demonstrate that the holmium laser pulse could in fact be rapidly terminated on command. This is demonstrated in Figure 12 where we present temporal waveforms for the full holmium pulse and a holmium pulse for which the beam was electronically shuttered at a selected delay time of ~ 50 μs. Shutter closure time after trigger pulse command was measured to be < 1 μs. Incomplete extinction of the laser beam upon shutter closure is due to: (1) nonoptimal setting of the high voltage pulse, which switches the Pockels cell, and (2) imperfect alignment of the second Glan laser polarizer with respect to the beam axis. Resource constraints at the end of the effort did not allow time for optimizing these settings. Such an optimization, which is a fairly straightforward engineering task, will be carried out in future work.

DISCUSSION

The results have demonstrated the applicability of utilizing the characteristic prompt optical emissions generated during Ho:YAG laser lithotripsy for the rapid automatic feedback control of laser energy delivery. The mechanics of the feedback control approach shown in Figure 1 are conceptually the same as those employed on the German "Lithognost" system (U.S. Patent No. 4,939,336) [10,12]. Both approaches require no

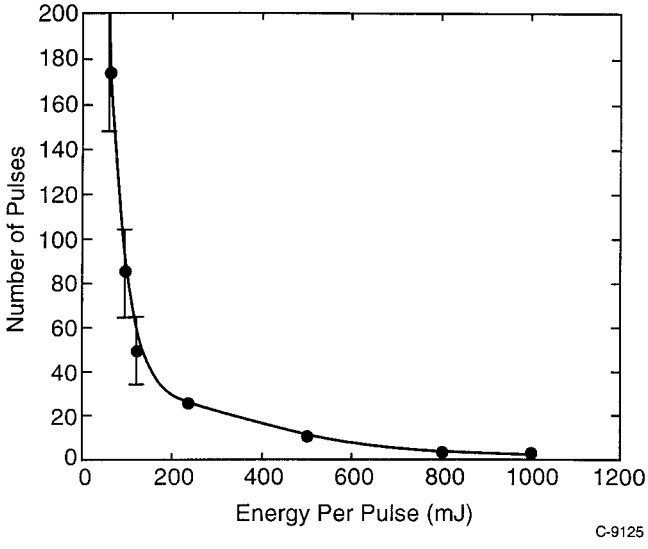

Fig. 11. Number of holmium pulses to perforate rabbit bladder wall (in vivo) 5 Hz PRF, 400 μm fiber, direct, near-normal contact.

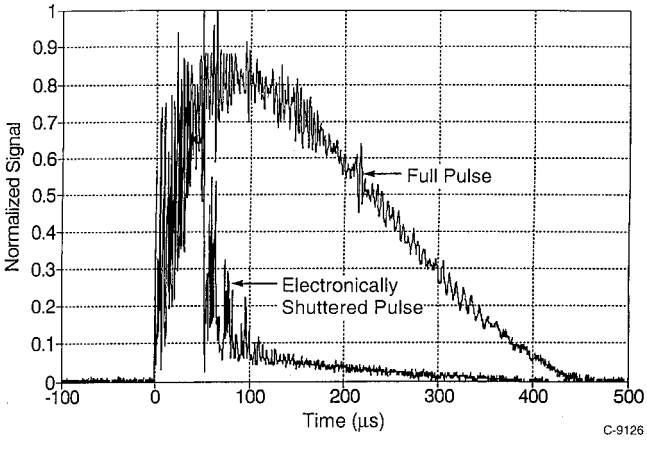

Fig. 12. Full and shuttered holmium laser pulse waveforms.

additional probe laser, utilize prompt optical emissions from the calculi for intrapulse feedback detection, and employ an electro-optic shutter for rapid intrapulse beam control. The difference between the approaches essentially lies in the specific stone/tissue discrimination algorithm each employs.

The German "Lithognost" system reportedly depends on differences between the laser-induced "fluorescence" emitted by calculi and soft tissue in the 650–1,000 nm range. Although the fluorophores responsible for the observed stone "fluorescence" have still not, to our knowledge, been identified, it is clear that such a detection algorithm will work only with lasers of excitation wavelength *less than* 1,000 nm. It would therefore *not* work with holmium laser excitation (λ = 2100 nm). Fluorescence detection has, of course, also been used in attempts to develop "smart" lasers for vascular surgery [13].

In contrast, the discrimination algorithm we have chosen to employ depends on distinct differences observed between the prompt laser-induced incandescence emitted by calculi and soft tissue. By incandescence we mean the thermally induced radiation emitted from the calculus surface itself or from a plasma-induced on it [10]. With this approach, as opposed to fluorescence detection, there is not the same restriction on laser excitation wavelength. The only requirement is that the laser wavelength be absorbed strongly enough by the calculus (or absorbing inclusions contained within) to generate a rapid and radiometrically measurable temperature rise. The applicability and viability of this stone/soft tissue detection algorithm to holmium laser excitation is supported by preliminary data shown in this report.

The data of the present study demonstrate that, for the majority of calculi, confirmation of whether the holmium laser is being discharged on a stone (versus soft tissue) is achievable within the first 120 mJ or less of deposited energy. This result in combination with the in vivo tissue safety data (Fig. 3 and 11), and the demonstration of intrapulse shuttering (Fig. 12), clearly point to the feasibility and potential value of the feedback control scheme we propose. In particular, the results suggest that our proposed scheme could yield an order of magnitude improvement in the holmium laser lithotriptor's margin of safety against soft tissue laser damage. This would enable a commercial laser lithotripsy system to be operated at the higher pulse energies most effective for rapid stone fragmentation while significantly reducing the risk of laser injury to surrounding urinary tract tissue.

Finally, holmium laser-induced photoemission signals from bone and cartilage suggest that a similar feedback scheme should be applicable to the automatic discrimination of cartilage from bone. This could help prevent, e.g., the unwanted laser ablation of underlying bone during arthroscopic chondroplasty procedures. To avoid ablating bone, the logic controlling the electronic shutter simply would be inverted from that used for lithotripsy. It would also reduce the risks of pressure wave damage to the fiber delivery and telescope device, which is known to occur when high pulse energies are discharged on bone. Discrimi-

nation of cartilage from surrounding soft tissue also appears possible.

The advantages of this method are considerable. In addition to offering increased tissue safety without compromising stone fragmentation efficacy, the particular optical feedback control scheme offers a number of specific advantages over other optical feedback control approaches. The scheme is based on robust incandescent optical signals inherent to pulsed laser ablation of calcific materials and the approach provides fast, automatic response during each laser pulse. Also the method requires no additional diagnostic laser; it uses the therapeutic laser to excite diagnostic signal and no expensive spectrum analyzers or computers to analyze diagnostic signal. In addition, the optical feedback signals are transmitted retrograde over laser delivery fiber with no extra diagnostic fibers needed.

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